

## FERUGINIDIN AND FERUGIN, TWO NEW SESQUITERPENOIDS BASED ON THE CAROTANE SKELETON FROM *FERULA JAESCHKEANA*<sup>1</sup>

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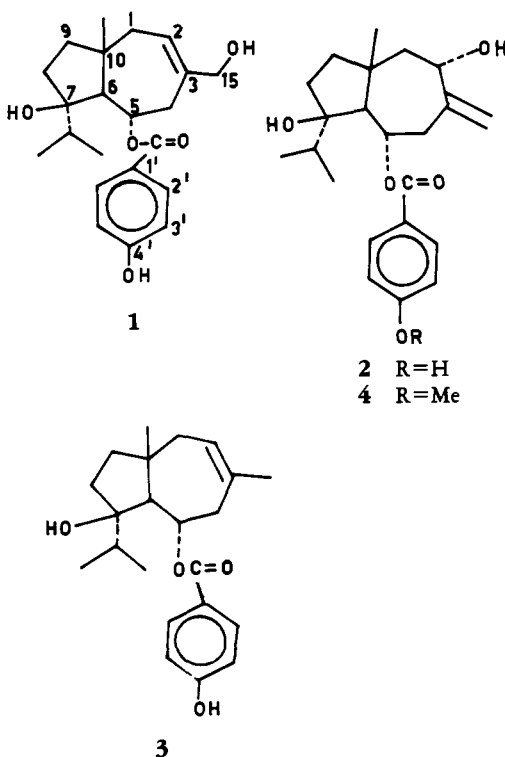
About seventy species of the large genus *Ferula* (Umbelliferae) have already been investigated chemically. Most of the widespread sesquiterpenes of *Ferula* species are derivatives of monocyclic and bicyclic sesquiterpenes having the germacrane, humulane, carotane, himachalane, or guaiane skeleton (1-3).

In continuation of our studies on *Ferula jaeschkeana* Vatke (4), two new compounds tentatively named feruginidin [1] and ferugin [2] were isolated and characterized.

The methanolic extract of *F. jaeschkeana* obtained after defatting the plant

material with light petroleum ether (40-60°) and C<sub>6</sub>H<sub>6</sub> was chromatographed on silica gel with elution by CHCl<sub>3</sub> and CHCl<sub>3</sub>/MeOH (5 to 10%) mixtures which resulted in three gross fractions D, E, and F. Fraction F on repeated chromatography on silica gel column using light petroleum ether (40-60°)/Me<sub>2</sub>CO (1 to 4%) mixtures followed by preparative tlc yielded two new compounds feruginidin [1] and ferugin [2].

Feruginidin [1], the 5 $\alpha$ -*p*-hydroxybenzoyl ester of jaeschkeanadiol and ferugin [2], the 5 $\alpha$ -*p*-hydroxybenzoyl ester of 2 $\alpha$ -hydroxy-3(15)-ene jaesch-



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keanadiol, both analyzed for molecular formulas C<sub>22</sub>H<sub>30</sub>O<sub>5</sub> and had mass spectra consistent with this composi-

tion. The uv maxima of both **1** and **2** (256 and 258 nm respectively), their ir bands at 3300-3350 (OH) and 1680  $\text{cm}^{-1}$  (ester), and their two pairs of two aromatic *ortho*-coupled protons indicated them to be an aromatic ester. Alkaline hydrolysis of **1** and **2** yielded *p*-hydroxybenzoic acid as one of the reaction products, confirming **1** and **2** as esters of this acid.

The ms of **1** and **2** showed a fragment at *m/z* 331 ( $\text{M}^+ - \text{C}_3\text{H}_7$ ) arising from the loss of an isopropyl group which is a typical loss in carotane sesquiterpenes with a hydroxy function at C-7(5). The  $^1\text{H}$ -nmr spectra (Table 1) of **1** and **2** were compared with a closely related sesquiterpene ester **3** (**6**) belonging to the carotane class of sesquiterpenes. Compound **1** had a signal for a hydroxymethyl group at  $\delta$  4.09 (br s) instead of for a vinylic methyl group at  $\delta$  1.84 (s) in **3**. Compound **2** exhibited a secondary hydroxyl group at C-2 which is assigned

the  $\alpha$ -stereochemistry on the basis of coupling constants of 6.0 Hz and 9.0 Hz between H-1 $\beta$  and H-2 $\beta$  and H-1 $\alpha$ , respectively. Compound **2** also showed signals for an exomethylene group at  $\delta$  4.93, 5.23 (br s) instead of the vinylic methyl group in **3**. The rest of the signals were similar to those of **3**, and were assigned on the basis of chemical shifts and  $^1\text{H}$ -nmr decouplings. The structure of **2** was further confirmed by comparing the  $^1\text{H}$ -nmr spectrum of its methyl ether [**4**] with that of the corresponding reported reaction product of epoxyjaeschkeanadiol *p*-hydroxy benzoate (**7**).

### EXPERIMENTAL

Mps are uncorrected. Uv spectra were recorded in MeOH.  $^1\text{H}$ -nmr spectra were taken at 400 MHz, TMS as internal standard. Eims and cims were obtained with a direct inlet system at 70 ev.

*F. jaeschkeana* rhizomes collected from Gulmarg (Kashmir) in November 1980 (voucher specimen No. 3013 preserved in the CIMAP herbarium), were air dried (1.6 kg), powdered, and

TABLE 1.  $^1\text{H}$  nmr of Feruginidin [**1**], Ferugin [**2**]<sup>a</sup>

| Proton Position        | Compounds             |                        |
|------------------------|-----------------------|------------------------|
|                        | Feruginidin (Hz)      | Ferugin (Hz)           |
| H-1a . . . . .         | 2.17, dd, (15, 6)     | 2.15, dd, (12, 6)      |
| H-1b . . . . .         | 1.57, dd, (15, 9)     | 1.30, dd, (12, 12)     |
| H-2 . . . . .          | 5.82, dd, (9, 6)      | 4.18, dd, (12, 6)      |
| H-4a . . . . .         | 2.48, dd, (15, 9)     | 2.64, dd, (15, 5)      |
| H-4b . . . . .         | 2.04, dd, (15, 5)     | 2.57, dd, (15, 5)      |
| H-5 $\alpha$ . . . . . | 5.20, ddd, (11, 9, 5) | 5.38, ddd, (12, 10, 4) |
| H-6 $\alpha$ . . . . . | 2.04, d, (11)         | 2.13, d, (10)          |
| H-8a . . . . .         | 1.25-1.59 m           | 1.3-1.65 m             |
| H-8b . . . . .         |                       |                        |
| H-9a . . . . .         |                       |                        |
| H-9b . . . . .         |                       |                        |
| H-11 . . . . .         | 1.94, qq, (7)         | 1.85, qq, (7)          |
| H-12 . . . . .         | 0.82, d, (7)          | 0.80, d, (7)           |
| H-13 . . . . .         | 0.93, d, (7)          | 0.89, d, (7)           |
| H-14 . . . . .         | 1.08, s               | 1.18, s                |
| H-15a . . . . .        | 4.09, brs             | 5.23, brs              |
| H-15b . . . . .        | —                     | 4.93, br s             |
| H-2' . . . . .         | 6.82, dd, (8.5, 2)    | 6.82, dd, (9, 2)       |
| H-3' . . . . .         | 7.88, dd, (8.5, 2)    | 7.85, dd, (9, 2)       |
| H-5' . . . . .         | 7.88, dd, (8.5, 2)    | 7.85, dd, (9, 2)       |
| H-6' . . . . .         | 6.82, dd, (8.5, 2)    | 6.82, dd, (9, 2)       |

<sup>a</sup>The assignments have been made on the basis of chemical shifts and  $^1\text{H}$  decouplings.

extracted in a Soxhlet Apparatus with light petroleum ether (40-60°), C<sub>6</sub>H<sub>6</sub>, and MeOH, respectively. Solvents were removed under vacuum yielding three different fractions A, B, and C. The methanolic extract (fraction C), a viscous mass (115 g) was chromatographed on SiO<sub>2</sub> (2 kg) with CHCl<sub>3</sub>, CHCl<sub>3</sub>-MeOH (95:5), CHCl<sub>3</sub>-MeOH (90:10), and CHCl<sub>3</sub>-MeOH (1:1) successively. Concentrated CHCl<sub>3</sub>-MeOH (90:10) eluate (8.0 g) was further chromatographed on SiO<sub>2</sub> column with light petroleum ether (40-60°)-Me<sub>2</sub>CO (96:4) followed by preparative tlc separation in CHCl<sub>3</sub>-MeOH (85:15), yielding two compounds named as feruginidin (Rf 0.62) and ferugin (Rf 0.55).

Both gave a reddish color when sprayed with 1% solution of vanillin-H<sub>2</sub>SO<sub>4</sub> on SiO<sub>2</sub>-tlc plates on heating (10 min at 100°).

**FERUGINIDIN.**—Compound [1] (30 mg) colorless needles (MeOH), mp 130°; C<sub>22</sub>H<sub>30</sub>O<sub>5</sub> (M+1, 375); uv λ max (MeOH) nm (log ε) 256 (4.12); (α)<sup>20</sup><sub>D</sub> + 6.0° (1.5, MeOH); ir (KBr) ν max 3350, 2950, 2930, 2870, 1680, 1610, 1590, 1510, 1450, 1380, 1160, 1100, 1030, 850 cm<sup>-1</sup>; <sup>1</sup>H nmr see Table 1; cims m/z (CH<sub>4</sub>, % rel. abundance) 375 (M+1) (2), 357 (M+1-H<sub>2</sub>O)<sup>+</sup> (38), 331 (M-C<sub>3</sub>H<sub>7</sub>)<sup>+</sup> (1), 279 (14), 235 (20), 219 (58), 202 (23), 201 (M+1-2 H<sub>2</sub>O-C<sub>6</sub>H<sub>4</sub> (OH) COOH)<sup>+</sup> (100), 200 (32), 175 (3), 157 (4.5), 127 (27), 75 (6); (Found C, 70.9; H, 8.16; C<sub>22</sub>H<sub>30</sub>O<sub>5</sub> require C, 70.58; H, 8.02).

**FERUGIN.**—Compound [2] (25 mg) colorless needles (MeOH), mp 140°; C<sub>22</sub>H<sub>30</sub>O<sub>5</sub> (356, M<sup>+</sup>-H<sub>2</sub>O); uv λ max (MeOH) nm (log ε) 258 (3.98); [α]<sup>20</sup><sub>D</sub> + 15.0° (1.5, MeOH); ir (KBr) ν max 3300, 2980, 2920, 2880, 1680, 1610, 1590, 1460, 1410, 1370, 1280, 1160, 1120, 1050, 920, 850 cm<sup>-1</sup>; ms m/z (% rel. abundance) 356 (M-H<sub>2</sub>O)<sup>+</sup> (20), 338 (M-2H<sub>2</sub>O)<sup>+</sup> (5), 331 (M-C<sub>3</sub>H<sub>7</sub>)<sup>+</sup> (6.5), 330 (40), 312 (40), 236 (M-C<sub>6</sub>H<sub>4</sub> (OH) COOH)<sup>+</sup> (5.5), 218 (4.5), 200 (20), 193 (M-C<sub>6</sub>H<sub>4</sub> (OH) COOH-C<sub>3</sub>H<sub>7</sub>)<sup>+</sup> (12), 175 (45), 157 (8), 132 (30), 121 (C<sub>6</sub>H<sub>4</sub> (OH) COOH-OH)<sup>+</sup> (100), 93 (25), 83 (5), 77 (5), 71 (25), 65 (70) (Found C, 70.80; H, 8.10; C<sub>22</sub>H<sub>30</sub>O<sub>5</sub> re-

quire C, 70.58; H, 8.02). Treatment of 2 with ethereal CH<sub>2</sub>N<sub>2</sub> afforded 4 identical with the product reported by Fraga *et al.* (7).

**HYDROLYSIS OF FERUGININ [1] AND FERUGIN [2].**—A mixture of 1 (10 mg) and 4% methanolic aqueous KOH (2 ml) was refluxed for 2 h. and worked up for the acidic fraction by the usual method.

The acidic fraction Rf 0.85 (C<sub>6</sub>H<sub>6</sub>-MeOH-HOAc, 90:16:8) showed one spot identical with an authentic sample of *p*-hydroxybenzoic acid, mp 210-214°. Similar hydrolysis of 2 also gave *p*-hydroxybenzoic acid.

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